

Contents lists available at [ScienceDirect](http://ScienceDirect.com)

Journal of Pediatric Surgery CASE REPORTS

journal homepage: www.jpascasereports.com

Granular cell tumor of the clitoris in the pediatric age. A case report and review of the literature

Maria Chiara Lucchetti^{a,*}, Hanadi Bakhsh^a, Francesca Bassani^a,
Francesca Diomedi Camassei^b^a Department of Nephrology and Urology, Pediatric Gynecology Unit, Bambino Gesù Pediatric Hospital, Rome, Italy^b Department of Laboratories, Pathology Unit, Bambino Gesù Pediatric Hospital, Rome, Italy

ARTICLE INFO

Article history:

Received 15 December 2014

Received in revised form

10 March 2015

Accepted 14 March 2015

Key words:

Granular cell tumor

Abrikossoff's tumor

Granular cell myoblastoma

Vulvar mass

Clitoral mass

Pediatric age

ABSTRACT

Granular cell tumors (GCTs) or Abrikossoff's tumors are rare, soft tissue tumors of neural origin with a generally benign behavior. They can occur anywhere in the body (with up to 7%–16% situated in the vulva) and can occur in patients of any age, being considered rare in children. A 6 year-old girl presented with a clitoral mass, surgically removed. Pathology revealed GCT of clitoris. To our knowledge this is the first case of GCT of the clitoris in the pediatric (prepubertal) age group reported in English literature. Although rare in pediatric age, GCT has to be suspected as a cause of vulvar mass. Surgical treatment and clinical follow-up must consider the possibility of recurrence, multiple location and malignancy with time.

© 2015 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Granular cell tumors (GCTs), initially described by Virchow and Weber in 1854 [1], are uncommon skin and soft tissue neoplastic lesions, occurring in less than 0.017–0.025% of all surgical specimens [1,2].

In 1926 Abrikossoff was the first to name a tongue localization of the tumor as 'granular cell myoblastoma,' because of its presumed skeletal muscle origin. Nowadays, electron microscopy and immunohistological studies generally support a Schwann cell origin [1–3], although the real histopathogenic mechanism of this condition is still unknown.

Other various cell types have then been implicated in the histogenesis of GCT, including smooth muscle cells, fibroblasts, and histiocytes [2].

GCTs are two or three times more common in females than in males, and black patients are more prevalent than whites [4]; although described in patients of any age, they are more frequently seen in the fourth to sixth decades of life, being rare in children [1]. Occasionally, familial and congenital occurrences have been reported [1,3,5].

Most GCTs are found in the head and neck region (45–65% of cases), with tongue being the most common location [2], but any organ can be involved: breast, respiratory system, gastrointestinal system, urinary system, female and male genitals, uvea, neurohypophysis and central and peripheral nervous system [5,6].

Five to 25% of patients have multiple (synchronous or metachronous) lesions, according to different series, and this wide range is probably related to the difference in the follow-up lengths. Multiple cutaneous GCTs are rare, especially in children and teenagers [3].

Female genital locations are rarely described (7%–16%) and the vulvar tumors are benign in 98% of cases, with only 2% reported as malignant [1]. A single case of vulvar malignant GCT in a 17-year-old patient is described in the Literature [7].

1. Case report

A healthy 6 year-old white girl was attended at the Pediatric and Adolescent Gynecology Clinic of the Bambino Gesù Pediatric Hospital for the evaluation of a clitoral mass. The mother stated that the swelling had been present in the clitoral area for approximately 3 months. There was no history of pain, enlargement, itching, discharge or bleeding from the mass.

* Corresponding author. Tel.: +39 066859 2396.

E-mail address: mchiara.lucchetti@opbg.net (M.C. Lucchetti).



Fig. 1. Preoperative appearance: enlarged clitoris, solid mass, normal skin.

The general physical examination was normal, with regional lymph nodes not enlarged, no clinical signs of sexual maturation, and vaginal mucosa not estrogenized. At the level of the clitoris (dorsal surface) a non tender, small, solitary, firm nodule measuring 2×1 cm diameter was present, with intact overlying skin (Fig. 1).

A pelvic ultrasound examination revealed no abnormalities and confirmed the absence of pubertal development, while a dense, homogenous, solid mass arising from the clitoris was superficially present. Primary differential diagnoses were sebaceous cyst versus dermoid cyst, and surgical removal under general anesthesia was indicated. Meantime, the patient was re-evaluated in another Hospital, where an attempt of aspiration of the mass was performed: it was unsuccessful and followed by local infection. One month later the patient came back to our Clinic; the mass appearance did not significantly differ from the previous clinical evaluation and the child was scheduled for surgery.

Surgical treatment was performed on a Day Surgery recovery, under general anesthesia; an excision of the skin surrounding the clitoris was performed with wide skin edges and complete removal of the mass (Fig. 2).

The post-operative course was uneventful and the patient was discharged few hours after the operation. Surgical pathology diagnosed a GCT of the clitoris. At a 4 years follow-up the girls is healthy, without evidence of local recurrence or other organs involvement.

2. Discussion

GCTs of the vulva are rare and generally benign. However, it is important for the pediatric gynecologist to be aware of their existence, in order to provide the patient with the appropriate management [1].



Fig. 2. Post operative appearance of external genitalia.

We were able to find 134 vulvar cases of GCTs in the Literature, with only 4 patients of prepubertal and adolescent age (6, 9, 17 and 18 years old, respectively) [1,8].

Out of the 5 cases of GCTs with clitoral involvement, indeed, only one case occurred in the adolescent age group [1]. To our knowledge, this is the first case of GCT of the clitoris in the pediatric, prepubertal age group reported in the English Literature.

Although rare, vulvar tumors are the most common variety of GCT encountered in the female genital region, accounting for 7–16% of all GCTs [1,4]. They have been documented to affect mainly the vulva, frequently involving the superficial portion of the labia majora [8]. Other uncommon reported sites in the female genital tract are the ovary, the uterine cervix [2], the perineum, the clitoris, the introitus, the perianal zone and the episiotomy scar [1].

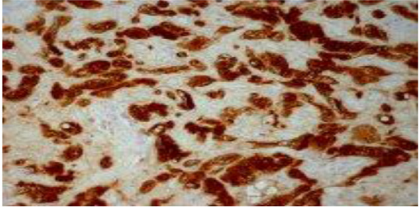
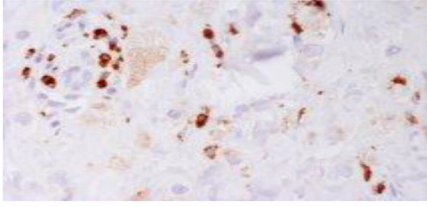
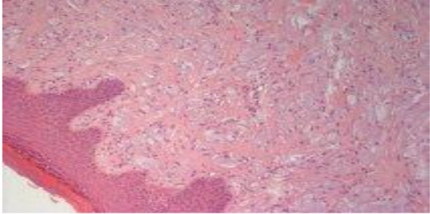
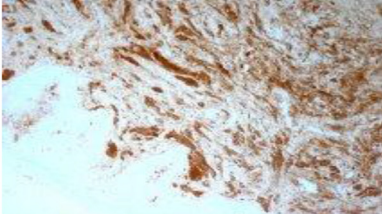
Recently, a case of benign GCT of the mons pubis in a 8-year-old girl has been reported as poster abstract (Clark N. et al.), in Journal of Pediatric Adolescent Gynecology, Volume 27, Issue 2 (April 2014) pages: e53–e54.

The most common clinical sign is the presence of an asymptomatic mass [1]; the lesion can be intradermal, submucosal, subcutaneous and appears as a superficial, solitary mass with firm texture, a non tender lump, rarely exceeding 4 cm in diameter [3]. Generally the swelling is mobile, slow growing over months or years, of pale whitish color, and the overlying skin may present depigmented, occasionally ulcerated or even thickened with a “cobblestone” appearance. Differential clinical diagnoses in case of female genital localization include sebaceous cyst, lipoma, fibroma, hidradenoma, papilloma, epidermal cyst, Bartholin's gland tumor, melanoma and hamartoma [4]. Ulcerative lesions sometimes complicating the larger cutaneous tumors can be confused with carcinomas or venereal diseases [1].

Correct preoperative diagnosis of GCT of the vulva is rare, it is often presumed to be a fibroma or sebaceous cyst, but histological examination through biopsy or excision is almost always correct and confirm the diagnosis [1].

At surgery, the tumor is non-encapsulated although well circumscribed, with a fleshy yellow-grey cut surface and ill defined margins [4]. Histologically, the tumor is composed by round-to-polyhedral cells with indistinct margins and granular, eosinophilic cytoplasm. The cells occur in ribbons or clumps, separated by a hyalinized stroma and collagen fibers. Nuclei are uniform, small and dark staining (Table 1a and b). The granular appearance is due to the accumulation of lysosomes. In almost an half of the cases the squamous epithelium overlying the tumor shows pseudoepitheliomatous

Table 1
Histopathology specimens of GCT.

 <p>Tab 1.a (10x): non-keratinizing squamous epithelium mucosa showed cellular proliferation of polygonal cells with abundant granular cytoplasm deep in the lamina propria.</p>	 <p>Tab 1.b (40x) higher magnification: enlarged cells with centrally located nucleus, clear or granular cytoplasm and indistinct cell membrane. No mitotic figures were observed.</p>
 <p>Tab 1.c (S100 10x): Same filed as Fig 1, immunostain with antibodies against S100 protein: strong positivity of proliferating cells.</p>	 <p>Tab 1.d (CD68 40x): anti-CD68 immunostain: few macrophages are positive whilst proliferating cells are negative or weakly positive.</p>

hyperplasia, which may be mistaken for squamous carcinoma. The cells are immunoreactive for S-100 protein (Table 1c), are periodic acid Schiff positive, diastase resistant and weakly positive for CD68 immunostain (Table 1d). The rare malignant cases may show necrosis, nuclear polymorphism and increased mitosis [4].

Other pathological entities may show similar histologic features as rhabdomyosarcoma, leiomyoma, myoblastoma, fibroma, lipoma, papilloma, hidradenoma, and some granular cell lesions associated with trauma or surgical injury.

The GCT, since not encapsulated, has a tendency to infiltrate the surrounding tissues, thus is mandatory to obtain uninvolved surgical margins (1–2 cm) for any kind and localization of this tumor by wide local excision, in order to minimize recurrences. If any evidence of microscopically involved surgical margin is detected, wider local excision should promptly be planned [5].

Recurrence rates are reported in 2–9% with clear margins and up to 20% with positive margins [4]. For malignant lesions the recurrence rate can reach 32%. Local recurrences usually appear within 2 years, thus strict follow-up after surgery is advisable for at least 2 years. Moreover, since the lesion has been reported to be multicentric in 4%–16% of cases, extragenital sites, particularly tongue and oral cavity, should be evaluated during the follow-up period. Although rare malignant variants have been reported,

recurrent GCT, despite benign histological features, may be the first indication of a potentially aggressive behavior [5]. Characteristic electron microscopic findings of intracytoplasmatic lysosomes have been described in such cases; then, wider local re-excision, and eventual radical vulvectomy with regional lymph nodes dissection should also be considered in those cases [5].

There is no role for adjuvant radiation or chemotherapy for benign GCTs.

3. Conclusion

GCT of the vulva in the pediatric and adolescent age group is an uncommon neoplasm. Although benign, it has a potential for multicentricity, recurrence, and possible aggressive malignant course, nonetheless malignant GCT has never been reported in pediatric age.

The treatment of choice is a wide local excision, with a previous, thorough, complete clinical exam in order to identify possible multiple tumors and familiar occurrences.

A meticulous follow-up for at least 2 years is needed to exclude local recurrences. Patients have to be alerted for possible, meta-chronous localizations with late onset.

Conflicts of interest

The authors indicate no conflicts of interest.

References

- [1] Kardhashi A, Deliso MA, Renna A, Trojano G, Zito FA, Trojano V. Benign granular cell tumor of the vulva: first report of multiple cases in a family. *Gynecol Obstet Invest* 2012;73(4):341–8. <http://dx.doi.org/10.1159/000336256>, PMID: 22517025.
- [2] Levavi Hanoch, Sabah Gad, Kaplan Boris, Tytiun Yehezkel, Braslavsky Diana, Gutman Haim. Granular cell tumor of the vulva: six new cases. *Arch Gynecol Obstet* 2006;273:246–9. <http://dx.doi.org/10.1007/s00404-005-0054-6>.
- [3] Golchai J, Zargari O, Paknejadi MB. Multiple granular cell tumor in a teenager: report of a case and review of the literature. *Acta Med Iran* 2004;42(3):228–31.
- [4] Rivlin Michel E, Meeks G Rodney, Ghafar Mohamed A, Lewin Jack R. Vulvar granular cell tumor. *World J Clin Cases* July 16, 2013;1(4):149–51.
- [5] Cohen Z, Kapuller V, Maor E, Mares AJ. Granular cell tumor (myoblastoma) of the labia majora: a rare benign tumor in childhood. *J Pediatr Adolesc Gynecol* 1999;12:155–6.
- [6] Godoy Guilherme, Mufarrij Patrick W, Tsou Hui C, Torre Pablo, Taneja Samir S. Granular cell tumor of scrotum: a Rare tumor of the male external genitalia. *Urology* 2008;72(3):716.e7–9.
- [7] Ramos PC, Kapp DS, Longacre TA, Teng NN. Malignant granular cell tumor of the vulva in a 17-year-old: case report and literature review. *Int J Gynecol Cancer* 2000;10:429–34.
- [8] Laxmisha C, Thappa DM. Granular cell tumour of the clitoris. *J Eur Acad Dermatol Venereol* 2007;21:392–3.